REMARKS

Favorable reconsideration is respectfully requested in view of the foregoing amendments and the following remarks.

I. CLAIM STATUS & AMENDMENTS

Claims 1 and 2 were pending in this application when last examined and stand rejected.

New claims 5-6 have been added as supported by the disclosure, for example, at page 3, lines 1-20, and pages 8-9, and original claims 1-2.

Claims 1-2 and 5-6 are pending upon entry of this amendment.

II. OBVIOUSNESS REJECTION

In item 7 on pages 3-5 of the Office Action, claims 1-2 were again remain rejected under 35 U.S.C. 103(a) as obvious over Scholler et al. (US 2003/0008342) in view of Yokoyama-Kobayashi et al. (Gene, Vol. 228, No. 1-2, pp. 161-167, March 1999).

This rejection is respectfully traversed as applied to claims 1-2 and new claims 5-6. The arguments set forth in the response filed April 13, 2007 are reiterated herein.

Applicants again respectfully submit that the novelty of the present invention is that "the C-terminal side of the transmembrane domain and the antigenic protein are outside of the cell." This means that a part of the transmembrane domain (C-terminal side thereof) and the antigenic protein are outside of the cell, and hence the "whole of the antigenic protein" is extracellularly expressed. No part of the antigenic protein is therefore anchored in the cell membrane.

As argued in the last response, this aspect of the invention is neither disclosed or suggested in the combined teachings of Scholler et al. and Yokoyama-Kobayashi et al., and more importantly, the cited references lack a reasonable expectation of success for combining/modifying their teachings to arrive at this aspect of the invention.

As noted in the last response, Scholler et al. relates to a study aimed to elicit or enhance the titer of antibodies specific for a cell surface receptor antigen (SRA). Though Scholler et al. discloses the possibility of "membrane localization" of an antigen for immune response (antibody

production, as noted in the last response, Scholler et al. do not show a concrete example of using transmembrane domain for the membrane localization and in the claimed method for producing antibodies.

In reply to this argument, the Office argued that US practice does not require Scholler et al. to provide a concrete example demonstrating the effectiveness of the teachings therein. Also, at the top of page 4 of the Office Action, it was indicated that Applicants have not provided evidence as to why Scholler et al. is not enabled.

In reply thereto, Applicants again respectfully submit that the lack of concrete examples is a factor to consider, especially when the combined cited prior art lacks a reasonable expectation of success as evidenced by the Boyle et al. reference attached to a previous response and discussed below. In addition, Applicants need not provide actual evidence that Scholler et al. is not enabled. Instead, Applicants are noting that the lack of a working example in Scholler et al. does not remedy the lack a reasonable expectation of success of the combined references when taken with the knowledge in the art.

As noted in the last response, Boyle et al. does provide a concrete example of the membrane localization. However, as noted in the last response, the state of the art as evidenced by Boyle et al., was such that membrane localization has disadvantages in terms of immune response (see, for example, the Abstract in Boyle et al.). Boyle et al. was previously submitted as evidence of the lack of a reasonable expectation of success in the art for producing antibodies using a fusion between a transmembrane domain and an antigenic protein. This is especially relevant in view of the uncertain suggestion in Scholler et al. In fact, the Boyle et al. shows negative results when compared to the present invention. All of this, would lead the skilled artisan to believe that such a fusion would decrease antibody production (which contravenes the purpose of the invention).

In reply thereto, the Examiner argued that Boyle et al. only discloses a slight increase in response to immunization with secreted versus membrane-bound antigen. The Office argued that Boyle et al. discloses that the antibody responses between mOVA and sOVA are equivalent at

the time of peak response. The Office further noted that the instant claims are not drawn to immunization. See page 4 of the Action.

Applicants respectfully disagree with the Office's positions.

The Office has argued that Boyle et al. disclose that antibody response between mOVA and sOVA are equivalent at the time of peak response. The Office relied upon the description at page 1900, first complete paragraph, lines 3-8, wherein Boyle et al. disclose:

> Compared to the response to sOVA, the IgG response of mOVA immunized mice was 30-fold lower at 2 weeks, but when it peaks at 8 weeks there was no significant difference from that of sOVA immunized mice (Fig. 2A) although the response in the sOVA immunized mice had reach a plateua.

Boyle et al. actually disclose that there was no significant difference between the IgG responses of mOVA and sOVA at 8 weeks. However, at 8 weeks, the response of mOVS was peak, while the response of sOVS had reached a plateau. That is, at the time of 8 weeks, the highest values for mOVA and the declined value of mOVS are compared, and they are estimated as being statistically equivalent.

More importantly, it is clear from Figs. 2-3 of Boyle et al. (at page 1900) that the total responses of the sOVA immunized mice are obviously higher than that of mOVA immunized mice.

The Examiner further argued that Boyle et al. disclose "[t]he IgG2a and IgG2b titers were similar between sOVA and mOVA immunized mice at all time points." This assertion appears to be based on Fig. 3 of Boyle et al.. Fig. 3 shows the clear difference in IgG1 titer between sOVA and mOVA. Regarding the IgG1a and IgG2b, actual titers with mOVA are clearly inferior to that with sOVA.

In view of this understanding of the state of the art, the skilled artisan would consider Boyle et al. as evidence of a lack of a reasonable expectation of success in the art for producing antibodies using a fusion between a transmembrane domain and an antigenic protein, based on the state of the art and the uncertain suggestion in Scholler et al.. As such, the skilled artisan would reasonably believe that such a fusion would decrease antibody production (which

contravenes the purpose of the invention). As such, it is respectfully submitted that the skilled artisan at the time of the invention would well recognize that immunization by membrane-type antigen should be less effective compared with that by secreted antigen.

Therefore, Boyle et al. is evidence that, at the time of filing of the application, it was believed that antibody titer decreases when using an antigenic protein, which has been converted into a membrane type by fusion with transmembrane domain. See again page 2, lines 13-20 of the specification and the Boyle reference (Int. Immunol., vol. 9, no. 12, pp. 1897-1906, 1997) discussed therein. Boyle et al. disclose that the membrane localization of antigen for immune response provides negative results.

In contrast to the results in Boyle et al., Applicants succeeded by fusing a non-membrane type antigenic protein with the C-terminal of the transmembrane domain, thereby localizing the protein to the cell surface, and producing positive results.

In fact, such an understanding of the state of the art would lead the skilled artisan away from the combination of Scholler et al. and Yokoyama-Kobayashi et al.

Accordingly, there was no reasonable expectation of success in the art for producing antibodies using a fusion between a transmembrane domain and an antigenic protein that is not naturally present on the surface of a cell, because based on the state of the art and the uncertain suggestion in Scholler, such a fusion would decrease antibody production.

Yokoyama-Kobayashi et al. fail to remedy the deficiencies in Scholler et al.

Though Yokoyama-Hashimoto et al. teach the claimed vector can be used to produce a fusion protein that can be used to anchor a secreted molecule to the cell surface, Yokoyama-Hashimoto et al. do not disclose that the claimed vector can express the fusion protein in a wholly extracellular mode.

Therefore, it is respectfully submitted that the present invention is neither disclosed nor suggested from the combined disclosures of Scholler et al. and Yokoyama-Hashimoto et al. and the cited references lack a reasonable expectation of success of combining and/or modifying their teachings to arrive at the claimed invention.

For these reasons, it is again respectfully submitted that claims 1-2 are novel and patentable over the combination of Scholler et al. and Yokoyama-Kobayashi et al.

Lastly, in the Office Action, it was indicated that the instant claims are not drawn to immunization or a particular route of immunization.

In reply, new claims 5-6 have been added, which are drawn to "immunizing of an animal" by "intradermal administration." It is respectfully submitted that such claims are neither disclosed nor suggested by the cited references, and that new claims 5-6 are or novel and patentable over the combined cited references for the same reasons set forth above with respect to claims 1-2.

In view of the above, the rejection of claims 1-4 under 35 U.S.C. § 103(a) over Scholler (US 2003/0008342) in view of Yokoyama-Kobayashi is untenable and should be withdrawn.

III. CONCLUSION

In view of the foregoing amendments and remarks, it is respectfully submitted that the present application is in condition for allowance and early notice to that effect is hereby requested.

If the Examiner has any comments or proposals for expediting prosecution, please contact the undersigned attorney at the telephone number below.

Respectfully submitted,

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